RESPONSE

The amendment to the specification corrects the issues raised in the final action in the prior case.

The specification is amended to provide the SEQ ID Nos. now required under U.S. Patent practice. The requirements for the nucleotide and/or amino acid sequences 37 CFR 1.821(a)(1) and (a)(2) are submitted herewith along with a computerized sequence listing ASCII text on diskette. The Cμ (mu) and Cγ (gamma) symbols are provided on page 31. The sequence ID numbers are added by amendment.

The Examiner has raised a variety of rejections based on § 112, and rejections under § 102 based on the asserted content of various prior art references. Each such rejection is addressed in turn.

1. The § 112 rejection regarding the use of the terms "class switching" cannot be maintained. The Examiner is not correct in stating that the new phrase is not defined in the prior art. The present application specifically refers to the prior art use of animals, specifically mice, whose immune system contains unrearranged human immunoglobulin loci, such as the mice described in U.S. Patent 5,874,299 and 6,139,835 and the process of class switching is expressly defined in that prior art.

The recitation in claim 10 as amended of "the lymphocytes of the chicken are comprised of the human immunoglobulin locus..." is not unclear. The B cell is not said to comprise a human chromosome as claimed, but to be comprised the human immunoglobulin locus. Again, this is completely consistent with the use of this terminology in the prior art. Because the term "locus" appears to be raising objections, Applicants have rephrased the pending claims to remove the term locus without changing the substantive meaning or content of the claims. Applicants have also specified that the genome of the lymphocytes is the site of the human immunoglobulin genes as

defined in the remainder of the claim.

The phrase "pseudo" in connection with the "pseudo v genes" is completely consistent with the use of the term in the prior art. The examples are numerous and readily ascertainable in the prior art. Examples of the accepted usage of the terms include:

Eur J Immunol. 1993 Oct;23(10):2448-53.
Polymorphism of the functional immunoglobulin variable region genes in the chicken by exchange of sequence with donor pseudogenes.

Benatar T, Ratcliffe MJ.
Mol Cell Biol. 1993 Feb;13(2):821-30.
Germ line maintenance of the pseudogene donor pool for somatic immunoglobulin gene conversion in chickens.

McCormack WT, Hurley EA, Thompson CB.
Mol Biol Evol. 1995 Jan;12(1):94-102.
Evolution of immunoglobulin VH pseudogenes in chickens.
Ota T, Nei M.

Claim 16 does not attempt to define any particular structure for a resulting IgG molecule after class switching. The definition of an IgG molecule is sufficient in and of itself to distinguish the class G isotope immunoglobulin molecule from those of other isotypes. The achievement of class switching from an immunoglobulin type M to an immunoglobulin type G is an important feature of the present invention. The difference between class M and class G is the result of class switching as claimed.

Applicants note that the difference between rearrangement and class switching is well recognized in the field of immunoglobulin gene rearrangement as evidenced by the '084 patent the Examiner cites. This language is conventional and the scope thereof readily discernable by one of ordinary skill in the art.

With respect to the cited prior art references, none of these disclose the application as claimed. The Rapp U.S. Patent Publication No. 2002/0108132-A12002 reference does not anticipate the pending claims. The present claims require that the genes undergo functional

immunoglobulin gene rearrangement. Rapp is directed to expression of a monoclonal antibody in a chicken and does not feature an animal having a population of B lymphocytes containing human immunoglobulin gene locus.

The examiner cites Example 11 of Buelow as prior art. However, this is fictitious data - BACs encompassing the chicken heavy chain locus do not exist. Similarly, Example 13 cites an "agammaglobulinemic " chicken. However, the cited chicken is not agammaglobulinemic - it is hypo-gammaglobulinemic (because they were selected for low concentrations of IgY) and only marginally so. The immune system of these birds is entirely normal. Hence, the "teachings" of Buelow are incorrect. Furthermore, transgenic chickens have never been made from embryonic stem cells despite 15 years of effort because conditions that allow the cells to colonize the germline have never been found (see van de Lavoir et al, 2006 Mechanisms of Development 123; 31-41). Taken together, Examples 13-15 show that Buelow's disclosure of a transgenic chicken that produces human immunoglobulins cannot meet the threshold of enablement to constitute an operative reference under 35 U.S.C. §102 or §103.

With respect to the rejection over Singh, U.S. Patent Publication No. 2002/0028488, as noted previously, the Singh publication is a farce. The copied United States patent relates only to expression of immunoglobulins in transgenic mice. Singh et al. is conspicuously non-enabling for the subject matter of the present claims because the specific gene modifications and restriction sites, etc., and essentially all functional portions of the Singh et al publication are directed to the mouse genome, not the chicken genome. Therefore, there is no ability to use Singh et al. to create the claimed subject matter can possibly exist.

Finally, the examiner states "All that is required in the applicant's claim is the production of a chimeric chicken which was well within the ability of the ordinary artisan". However, a chimeric chicken carrying a transgene was first made in 2004 which is three years after the Buelow application

was filed. The novelty of making a transgenic chimera was recognized by the patent office in US 7145057. Clearly, making a transgenic chimera was not within the ability of an ordinary artisan.

Therefore, none of the prior art references anticipates the present claims.

The Commissioner is also authorized to $525.00 for the three month extension fee to Orrick Herrington & Sutcliffe's Deposit Account No. **150665** and charge any fees required by the filing of this papers, and to credit any overpayment to Orrick Herrington & Sutcliffe's Deposit Account No. **150665.**

Respectfully submitted,

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By: _____

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